

Research Progress on Eradicating *Helicobacter pylori* to Prevent Gastric Cancer

Yan Jiang¹, Jian Pang², Jingyu Wu², Chen Sun², Tengqi Wang^{2*}

¹Inner Mongolia Medical University, Hohhot 010000, Inner Mongolia Autonomous Region, China

²Department of Gastrointestinal Surgery, Bayannur Hospital, Bayannur 015000, Inner Mongolia Autonomous Region, China

*Corresponding author: Tengqi Wang, wangtengqi@bynesyy.com

Copyright: © 2023 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Gastric cancer is a malignant tumor that originates in the gastric mucosal epithelium. It mainly occurs in people over 50 years old. With the increasing work pressure, *Helicobacter pylori* infection, and other factors, gastric cancer patients are also getting younger. Gastric cancer has no obvious symptoms in its early stages. Therefore, gastric cancer patients are often diagnosed at the middle and late stages of the disease. The prognosis and survival rate of gastric patients are not ideal. Therefore, prevention should be taken for people who are at risk of getting gastric cancer. *Helicobacter pylori* is a significant cause of the occurrence and development of gastric cancer. The bacterium produces various virulence factors, triggering the Correa cascade reaction, ultimately culminating in the development of gastric cancer. Clinically, it is believed that eradication of *Helicobacter pylori* can reverse precancerous lesions of the stomach and therefore prevent gastric cancer, but it has not been confirmed yet. This article explores explicitly the research progress on eradicating *Helicobacter pylori* in the context of gastric cancer prevention.

Keywords: *Helicobacter pylori*; Eradication methods; Gastric cancer prevention; Atrophic gastritis

Online publication: December 26, 2023

1. Introduction

Helicobacter pylori is a type I gram-negative bacterium that is spiral-shaped (spirillum). *Helicobacter pylori* can infect the human gastric mucosa, and the environment in which it grows is microaerobic. *Helicobacter pylori* is highly contagious and is mainly transmitted orally or through feces. Globally, there are a vast number of people infected with *Helicobacter pylori*. According to incomplete statistics, about 10 million people in China are infected with *Helicobacter pylori*, accounting for 20% to 30% of the world's total. *Helicobacter pylori* can accelerate the development of various gastric-related diseases, which may eventually develop into gastric cancer. B-cell mucosa-associated lymphoid tissue lymphoma and peptic ulcer are some of the more common causes of gastric diseases. The role of *Helicobacter pylori* in promoting the occurrence and development of gastric cancer has been clinically proven, and it is also a significant cause of gastric cancer^[1]. As early as 1994, the World Health Organization listed *Helicobacter pylori* as a Class I carcinogen. Carrying out eradication

treatment can better prevent the occurrence of gastric cancer. When infected by *Helicobacter pylori*, the human body will secrete many pathogenic factors, among which cytotoxin-related factor A and vacuolated cytotoxin A are two of the more common ones. With the secretion of these pathogenic factors, the antioxidant function and protein connection function of the gastric mucosa will be affected. The imbalance of these pathogenic factors will ultimately induce gastric cancer. However, there is still considerable clinical controversy about whether eradicating *Helicobacter pylori* can prevent gastric cancer, so further research is needed.

2. The mechanism by which *Helicobacter pylori*-related virulence factors lead to gastric cancer

2.1. Vacuolating cytotoxin A and the pathogenesis of gastric cancer

Helicobacter pylori is produced by various virulence factors, of which vacuolating cytotoxin A is typical. This toxin can form a selective ion channel for *Helicobacter pylori*, feeding off the products of metabolism and electrolytes in human cells. This mechanism allows *Helicobacter pylori* to survive. Vacuolating cytotoxin A causes the cytoplasm to transform into vacuoles gradually, further affecting the target cells' functions, such as interfering with the mitochondrial membrane and stimulating cell apoptosis [2]. Relevant studies [3] have shown that when the human body is infected with *Helicobacter pylori* and there is a presence of vacuolating cytotoxin A, the level of cytotoxin-related gene A will increase.

Cytotoxin-related factor A is another virulence factor associated with *Helicobacter pylori*. This additional virulence factor accumulates in gastric epithelial cells due to the influence of vacuolating cytotoxin A. Over time, this accumulation can lead to the development of gastric cancer. Another clinical study analysis [4] showed that the patients who were negative for vacuolating cytotoxin A antibodies were at higher risk of developing gastric cancer compared to patients who were positive for cytotoxin A antibodies. Therefore, there is a significant correlation between the occurrence of gastric cancer and vacuolating cytotoxin A.

2.2. Cytotoxin-related gene A and the pathogenesis of gastric cancer

Cytotoxin-related gene A is a virulence factor secreted by *Helicobacter pylori*. The protein of this virulence factor can reach gastric epithelial cells based on the type IV secretion system. The C-terminus of cytotoxin-related gene A appears tyrosine phosphorylated, which is fatal. Scaffolding proteins may also be formed as a result, and there are independent and dependent cases of amino acid phosphorylation. Still, in either case, they will interact with signaling proteins in the human body, and the cells in the human body will be continuously induced to undergo morphological changes. Changes in this aspect increase cell energy, hindering their normal movement and proliferation and ultimately leading to cancer development. Research indicates that the induction of cytotoxin-related gene A can lead to the polarization of epithelial cells, causing a shift in the phenotype towards a more invasive aspect. When working in conjunction with cancer-promoting proteins and *Helicobacter pylori*, cytotoxin-related gene A contributes to an increased expression of itself in human gastric epithelial cells. Ultimately, this process can induce gastric cancer. Moreover, abnormal expression of cytotoxin-related gene A can result in cancerous damage or genetic instability, further contributing to the development of gastric cancer [5].

3. Research progress on the role of *Helicobacter pylori* eradication in preventing gastric cancer

3.1. Progress in the prevention of non-atrophic gastritis by eradicating *Helicobacter pylori*

Once infected with *Helicobacter pylori*, patients are prone to chronic non-atrophic gastritis. *Helicobacter pylori* can be found in patients with gastritis through examinations. At the same time, they will also experience

structural changes in the gastric mucosa. *Helicobacter pylori* has multiple effects on the human gastric mucosa. Firstly, patients infected with *Helicobacter pylori* will experience chronic non-atrophic gastritis, which will develop into acute gastritis. If *Helicobacter pylori* is eradicated, the inflammation will gradually subside. If *Helicobacter pylori* is not eliminated, the number of parietal cells that secrete gastric acid and the main cells that secrete digestive enzymes will continue to decrease, eventually leading to atrophy of the gastric mucosa. Atrophic gastritis is a lesion before gastric cancer that will significantly increase the risk of gastric cancer. Some scholars ^[6] conducted a group test patients who tested positive for *Helicobacter pylori* and randomly divided these patients into an eradication group and a control group. Patients in the eradication group underwent *Helicobacter pylori* eradication treatment, and patients in the control group underwent placebo treatment. Then, the patients were followed up for seven years. After seven years, none of the patients who did not develop atrophic gastritis developed gastric cancer. Meanwhile, among the patients in the control group who did not have atrophic gastritis, six of them developed gastric cancer. This indicates that the incidence of gastric cancer in non-atrophic gastritis patients can be effectively reduced through the eradication of *Helicobacter pylori*.

3.2. Progress in *Helicobacter pylori* eradication in preventing atrophic gastritis

Patients with atrophic gastritis exhibit chronic inflammation in the gastric mucosa, accompanied by significant atrophy in the gastric glands. The patient's lesions may have fibrosis, intestinal metaplasia, or pseudopyloric metaplasia. Statistics ^[7] show that patients who are positive for *Helicobacter pylori* are five times more likely to develop atrophic gastritis compared to patients who are negative for *Helicobacter pylori*. This shows that *Helicobacter pylori* infection is closely related to atrophic gastritis development. In patients with atrophic gastritis, the two virulence factors of *Helicobacter pylori* are closely associated with gastric mucosa atrophy. *Helicobacter pylori* induces various inflammatory factors through bacterial oxidation, leading to their accumulation in the gastric mucosa. Therefore, gastric epithelial cell damage is prone to occur. Clinical follow-up of patients with atrophic gastritis five years later found that after successfully eradicating *Helicobacter pylori*, gastric mucosal atrophy was significantly reduced, and the patient's mucosa could eventually heal. However, whether the eradication of *Helicobacter pylori* can prevent atrophic gastritis from developing further into gastric cancer is still debatable. According to relevant literature ^[8], patients with atrophic gastritis who do not exhibit intestinal metaplasia did not develop gastric cancer after the eradication of *Helicobacter pylori*. In contrast, among patients with atrophic gastritis and intestinal metaplasia, some individuals still developed gastric cancer after the eradication of *Helicobacter pylori*. Therefore, this shows that the eradication of *Helicobacter pylori* might be effective in preventing gastric cancer in certain groups of patients. For patients with mild atrophic gastritis, the *Helicobacter pylori* eradication can effectively prevent the occurrence of gastric cancer. However, this treatment might not be effective in preventing gastric cancer for patients with moderate to severe atrophic gastritis. Therefore, for patients with atrophic gastritis, it is necessary to promptly evaluate the degree of gastric mucosal lesions and carry out *Helicobacter pylori* eradication treatment as early as possible to improve the gastric mucosal lesions better, to reduce the risk of gastric cancer effectively ^[9].

3.3. Progress in the prevention of intestinal metaplasia by eradicating *Helicobacter pylori*

Intestinal metaplasia refers to the replacement of the human gastric mucosa with epithelium resembling that of the small intestine mucosa. Intestinal metaplasia is often caused by the stimulation of persistent inflammation in the gastric mucosa, and patients infected with *Helicobacter pylori* have persistent inflammation. Persistent inflammation plays a crucial role in intestinal metaplasia, which is closely related to the occurrence of gastric cancer. Therefore, to prevent the occurrence of gastric cancer, it is also necessary to avoid intestinal metaplasia. A retrospective study ^[10] showed that about 42% of gastric cancer patients included in the study had intestinal epithelial changes, and about

17% of these patients showed severe mucosal lesions and intestinal epithelial changes. Notably, these patients not only presented with larger tumors but also had a higher incidence of submucosal invasion. This shows that intestinal metaplasia is an essential factor in the occurrence and development of gastric cancer.

4. Conclusion

In summary, *Helicobacter pylori* plays a vital role in the occurrence and development of gastric cancer, and more and more clinical evidence has confirmed that the eradication of *Helicobacter pylori* can effectively reduce the risk of gastric cancer. Although the eradication of *Helicobacter pylori* has a significantly lower anti-cancer effect in patients with severe intestinal metaplasia and atrophic gastritis, the sooner *Helicobacter pylori* eradication treatment is carried out, the more effective it is for the patient. By further exploring the connection between *Helicobacter pylori* and gastric cancer and carrying out *Helicobacter pylori* eradication treatment as early as possible the incidence of clinical gastric cancer can be effectively reduced, protecting the lives of patients.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Yin S, Wang S, Li A, et al., 2023, Research Progress on Eradicating *Helicobacter pylori* to Prevent Gastric Cancer. *Guangxi Medicine*, 45(2): 212–214.
- [2] Chu L, Wang N, Hao J, et al., 2023, Research Progress on Polyamines and *Helicobacter pylori*-Related Gastric Cancer. *International Medical and Health Herald*, 29(20): 2848–2851.
- [3] Sun T, Ke X, Wang Q, 2022, Research Progress on Metachronous Gastric Cancer Related to *Helicobacter pylori* Infection. *International Journal of Gastroenterology*, 42(3): 4.
- [4] Wang J, Zhang J, 2023, Research Progress on the Drug Resistance Mechanism of *Helicobacter pylori*. *Progress in Clinical Medicine*, 13(7): 10694–10699.
- [5] Wang D, Yan X, Zhang Y, 2023, Research Progress on the Impact of *Helicobacter pylori* Infection on Gastric Cancer Immunotherapy. *Chinese Clinical Pharmacology and Therapeutics*, 28(2): 228–234.
- [6] Xu X, He C, Zhu Y, 2022, New Progress in the Prevention and Treatment of *Helicobacter pylori* and Gastric Cancer. *Shanghai Medicine*, 45(11): 791–794.
- [7] Yang N, Shen J, Shao X, 2023, Study on the Impact of *Helicobacter pylori* Eradication on the Incidence of Metachronous Gastric Cancer After Endoscopic Resection of Early Gastric Cancer. *Zhejiang Medicine*, 45(1): 97–101.
- [8] Zhou X, Du Y, 2022, Preventing and Treating *Helicobacter pylori* Infection is the Only Way to Prevent Gastric Cancer. *Journal of Naval Medical University*, 43(12): 7.
- [9] Xiao R, Tao S, Chen S, et al., 2023, Research Progress on the Involvement of *Helicobacter pylori* in the Invasion and Metastasis of Gastric Cancer. *Journal of Shanghai Jiao Tong University: Medical Edition*, 43(4): 495–499.
- [10] Xu F, Chen Z, Deng C, et al., 2023, Research Progress on the Correlation Between *Helicobacter pylori* and Early Gastric Cancer. *Journal of Southwest Medical University*, 46(2): 122–125.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.